

Patent claims

1. In vitro method for the production of a homologous heart valve, comprising the following steps:

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- provision of a biodegradable support (scaffold),
- colonization of the support with homologous fibroblasts and/or myofibroblasts to form a connective tissue matrix,
- optionally colonization of the connective tissue matrix with endothelial cells
- fixing of the matrix to a non-degradable or poorly degradable frame construction (stent),

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wherein, before and/or after the fixing to the frame construction, the connective tissue matrix optionally colonized with endothelial cells is introduced into a pulsatile flow chamber in which it can be exposed to increasing flow rates, and the flow rate is increased continuously or discontinuously.

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2. In vitro method for the production of a homologous heart valve, comprising the following steps:

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- provision of a biodegradable support (scaffold) which is firmly connected to a non-degradable or poorly degradable frame construction (stent),
- colonization of the support with homologous fibroblasts and/or myofibroblasts to form a connective tissue matrix,
- optionally colonization of the connective tissue matrix with endothelial cells,
- introduction of the frame construction with the connective tissue matrix connected thereto into a pulsatile flow chamber in which it can be exposed to increasing flow rates,
- continuous or discontinuous increasing of the flow rate.

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3. Method according to one of claims 1 to 2, characterized in that the biodegradable support is a biodegradable polymer matrix or an acellular biological matrix.
4. Method according to one of claims 1 to 3, characterized in that the support is a polyglycolic acid (PGA), polylactic acid (PLA), polyhydroxyalkanoate (PHA), poly-4-hydroxybutyrate (P4HB) or a mixture of two or more of these polymers.
5. Method according to one of claims 1 to 4, characterized in that the support has a polymer density of 40 to 120 mg/cm³, preferably 50 to 80 mg/cm³.
- 10 6. Method according to one of claims 1 to 5, characterized in that the support is a porous polymer having a pore size of 80 to 240 µm.
7. Method according to one of claims 1 to 6, characterized in that the fibres of the support have a diameter of 6 to 20 µm, preferably 10 to 18 µm.
- 15 8. Method according to one of claims 1 to 7, characterized in that the support is a connective tissue framework of an animal or human heart valve.
- 20 9. Method according to one of claims 1 to 8, characterized in that the step of colonization with fibroblasts and/or myofibroblasts is repeated 3 to 14 times, preferably 5 to 10 times.
- 25 10. Method according to one of claims 1 to 9, characterized in that approx. 10⁵ to 6 x 10⁸ fibroblasts and/or myofibroblasts are employed per square centimetre of support/matrix and colonization step.
11. Method according to one of claims 1 to 10, characterized in that the step of colonization with endothelial cells is repeated 3 to 14 times, preferably 5 to 10 times.
- 30 12. Method according to one of claims 1 to 11, characterized in that approx. 10⁵ to 5 x 10⁸ endothelial cells are employed per square centimetre of support/matrix and colonization step.

13. Method according to one of claims 1 to 12, characterized in that the fibroblasts and/or myofibroblasts and/or endothelial cells are human cells.
- 5 14. Method according to one of claims 1 to 13, characterized in that the fibroblasts and/or myofibroblasts and/or endothelial cells are autologous cells.
15. Method according to one of claims 1 to 14, characterized in that the frame construction is made of a biocompatible non-degradable material.
- 10 16. Method according to one of claims 1 to 15, characterized in that the frame construction is made of a biocompatible poorly degradable material.
- 15 17. Method according to one of claims 1 to 16, characterized in that the support is fixed to the frame construction by means of conventional suturing and/or fibrin adhesive.
18. Method according to one of claims 1 to 17, characterized in that flow rates of 5 ml/min to 8,000 ml/min, preferably 50 to 2,000 ml, are established in the pulsatile flow chamber.
- 20 19. Method according to one of claims 1 to 18, characterized in that the flow rate is increased over a period of 1 week to 12 weeks.
- 25 20. Method according to one of claims 1 to 19, characterized in that the initial flow rate is 50 to 100 ml/min.
21. Method according to one of claims 1 to 20, characterized in that the initial pulse frequency is 5 to 10 pulses/min.
- 30 22. Method according to one of claims 1 to 21, characterized in that the flow rate is increased to 5,000 ml/min.

23. Method according to one of claims 1 to 22, characterized in that the pulse frequency is increased to 180 pulses/min.
24. Method according to one of claims 1 to 23, characterized in that systemic pressures of 5 10 to 240 mm Hg are established in the pulsatile flow chamber.
25. Autologous heart valve, characterized in that it has been produced by a method according to one of claims 1 to 24.
- 10 26. Autologous heart valve having a connective tissue inner structure surrounded by an endothelial cell layer, characterized in that it is fixed to a non-degradable or slowly degradable frame construction (stent).
- 15 27. Autologous heart valve according to claim 26, characterized in that a collagen density of 20 to 60 % exists in the connective tissue core.
28. Autologous heart valve according to claim 27, characterized in that it withstands the flow conditions in the human heart.